

REMARKS

The precise changes being made by the claim amendments are set forth in the marked up version of the amended claims presented in an Appendix hereto. In order to clearly show the changes, in the appendix all introduced material is shown underlined, thus: introduced material and deletions are shown as strikethrough or brackets, thus: ~~strikethrough~~ or [].

No new matter has been introduced by the above amendments. The claims are in condition for allowance. A Notice of Allowance is earnestly requested.

Respectfully Submitted,

June 20, 2002

By 

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APPENDIX**Version with markings to show changes made**

The amendments have been made as follows:

In the specification, first paragraph, page 1, lines 3 to 10:

This application claims priority to foreign patent Application Number 0103650-8, filed in Sweden on November 02, 2001 which is pending and it also claims priority to U.S. Provisional Patent Application Number 60/262,107 filed on January 16, 2001. This patent application is co-pending with PCT Application No. [] PCT/SE02/00068 filed on ~~even date herewith~~ January 15, 2002 in European Patent Office in Sweden. This invention relates to novel 8-amino derivatives, methods for their preparation, pharmaceutical compositions containing them and their use in therapy.

In the Claims:

1. (**Amended**) A compound selected from: 8-(4-methyl-1-piperazinyl)-*N*-[4-(4-morpholinyl)phenyl]-4-oxo-4*H*-chromene-2-carboxamide;
- 2-{ 1-[4-(2-Methoxy-phenyl)-piperazin-1-yl]-methanoyl }-8-(4-methyl-piperazin-1-yl)-chromen-4-one;
- 2-{ 1-[4-(1-Acetyl-2,3-dihydro-1*H*-indol-6-yl)-piperazin-1-yl]-methanoyl }-8-(4-methyl-piperazin-1-yl)-chromen-4-one;
- 2-Chloro-5-(4-{ 1-[8-(4-methyl-piperazin-1-yl)-4-oxo-4*H*-chromen-2-yl]-methanoyl }-piperazin-1-yl)-benzonitrile;
- 2-{ 1-[4-(4-Methoxy-phenyl)-piperazin-1-yl]-methanoyl }-8-(4-methyl-piperazin-1-yl)-chromen-4-one;
- 8-(4-Methyl-piperazin-1-yl)-4-oxo-4*H*-chromene-2-carboxylic acid (5-furan-2-yl-1*H*-pyrazol-3-yl)-amide;
- 8-(4-Methyl-piperazin-1-yl)-4-oxo-4*H*-chromene-2-carboxylic acid (4-imidazol-1-yl-phenyl)-amide;
- 8-(4-Methyl-piperazin-1-yl)-4-oxo-4*H*-chromene-2-carboxylic acid (4-[1,2,3]thiadiazol-5-yl-phenyl)-amide;
- 8-(4-Methyl-piperazin-1-yl)-4-oxo-4*H*-chromene-2-carboxylic acid 4-[1,2,3]thiadiazol-5-yl-benzylamide;
- 8-(4-Methyl-piperazin-1-yl)-4-oxo-4*H*-chromene-2-carboxylic acid [4-(4-acetyl-piperazin-1-yl)-phenyl]-amide;

8-(4-Methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid [4-(4-methanesulfonyl-piperazin-1-yl)-phenyl]-amide;

8-(4-Methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (2-methoxy-4-morpholin-4-yl-phenyl)-amide;

8-(4-Methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (3-chloro-4-morpholin-4-yl-phenyl)-amide;

8-(4-Methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (4-thiomorpholin-4-yl-phenyl)-amide;

8-(4-Methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (2,5-diethoxy-4-morpholin-4-yl-phenyl)-amide;

8-(4-Methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (4-cyanomethyl-phenyl)-amide;

8-(4-Methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (1H-indol-5-yl)-amide;

8-(4-Methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid [4-(1-morpholin-4-yl-methanoyl)-phenyl]-amide;

8-(4-Methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid [4-(2,6-dimethyl-morpholin-4-yl)-phenyl]-amide;

8-(4-Methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid [4-(4-fluoro-phenoxy)-phenyl]-amide;

8-(4-Methyl-piperazin-1-yl)-2-(6-morpholin-4-yl-benzooxazol-2-yl)-chromen-4-one;

8-(4-Methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (2-hydroxy-4-morpholin-4-yl-phenyl)-amide;

8-(4-Methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (5-ethoxy-benzothiazol-2-yl)-amide;

8-(4-Methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (4-bromo-phenyl)-amide;

8-(4-Methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid methyl-(4-morpholin-4-yl-phenyl)amide;

8-(4-Methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (3-morpholin-4-yl-phenyl)-amide;

8-(4-Methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (3-cyano-4-morpholin-4-yl-phenyl)-amide;

8-(4-Methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-amide;

4-[4-({ 1-[8-(4-Methyl-piperazin-1-yl)-4-oxo-4H-chromen-2-yl]-methanoyl }-amino)-phenyl]-piperazine-1-carboxylic acid *tert*-butyl ester;

8-(4-Methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (4-piperazin-1-yl-phenyl)-amide;

6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (4-morpholin-4-yl-phenyl)-amide;

6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid [4-(4-methanesulfonyl-piperazin-1-yl)-phenyl]-amide;

6-Methoxy-8-(4-Methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (3-chloro-4-morpholin-4-yl-phenyl)-amide;

6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-amide;

6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (2-methoxy-4-morpholin-4-yl-phenyl)-amide;

6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (4-thiomorpholin-4-yl-phenyl)-amide;

6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid [4-(2,6-dimethyl-morpholin-4-yl)-phenyl]-amide;

6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (3-morpholin-4-yl-phenyl)-amide;

6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid {4-[4-(2-hydroxy-ethyl)-piperazin-1-yl]-phenyl}-amide;

6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid [4-(1-morpholin-4-yl-methanoyl)-phenyl]-amide;

6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (3-cyano-4-morpholin-4-yl-phenyl)-amide;

4-[4-({1-[6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromen-2-yl]-methanoyl}-amino)-phenyl]-piperazine-1-carboxylic acid *tert*-butyl ester

6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (4-piperazin-1-yl-phenyl)-amide;

6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid [4-(4-propionyl-piperazin-1-yl)-phenyl]-amide;

6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid [4-(4-ethane sulfonyl-piperazin-1-yl)-phenyl]-amide;

6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid [4-(4-dimethyl sulfamoyl-piperazin-1-yl)-phenyl]-amide;

4-[4-({1-[6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromen-2-yl]-methanoyl}-amino)-phenyl]-piperazine-1-carboxylic acid dimethylamide;

4-[4-({1-[6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromen-2-yl]-methanoyl}-amino)-phenyl]-piperazine-1-carboxylic acid ethylamide;

4-[4-({1-[6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromen-2-yl]-methanoyl}-amino)-phenyl]-piperazine-1-carboxylic acid cyclohexylamide;

4-[4-({1-[6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromen-2-yl]-methanoyl}-amino)-phenyl]-piperazine-1-carboxylic acid cyclopentylamide;

6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid {4-[4-(1-pyrrolidin-1-yl-methanoyl)-piperazin-1-yl]-phenyl}-amide;

6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid {4-[4-(propane-2-sulfonyl)-piperazin-1-yl]-phenyl}-amide;

6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid {4-[4-(2-methyl-propanoyl)-piperazin-1-yl]-phenyl}-amide;

6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid {4-[4-(1-morpholin-4-yl-methanoyl)-piperazin-1-yl]-phenyl}-amide;

6-Fluoro-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (4-morpholin-4-yl-phenyl)-amide;

6-Fluoro-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid [4-(4-methanesulfonyl-piperazin-1-yl)-phenyl]-amide;

6-Fluoro-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid [4-(4-acetyl-piperazin-1-yl)-phenyl]-amide;

6-Fluoro-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (3-chloro-4-morpholin-4-yl-phenyl)-amide;

6-Fluoro-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-amide;

6-Fluoro-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (3-cyano-4-morpholin-4-yl-phenyl)-amide;

6-Fluoro-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid [4-(1-morpholin-4-yl-methanoyl)-phenyl]-amide;

6-Methyl-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (4-morpholin-4-yl-phenyl)-amide;

6-Methyl-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid [4-(1-morpholin-4-yl-methanoyl)-phenyl]-amide;

6-Methyl-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-amide;

6-Chloro-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (4-morpholin-4-yl-phenyl)-amide;

5-Methyl-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (4-morpholin-4-yl-phenyl)-amide;

5-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (4-morpholin-4-yl-phenyl)-amide;

6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid {4-[4-(3-hydroxy-propanoyl)-piperazin-1-yl]-phenyl}-amide;

4-[4-({1-[6-Fluoro-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromen-2-yl]-methanoyl}-amino)-phenyl]-piperazine-1-carboxylic acid *tert*-butyl ester;

4-[4-({1-[6-Fluoro-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (4-piperazin-1-yl-phenyl)-amide];

6-Fluoro-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid [4-(4-ethane sulfonyl-piperazin-1-yl)-phenyl]-amide;

6-Fluoro-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid [4-(4-propionyl-piperazin-1-yl)-phenyl]-amide; and

6-Fluoro-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid {4-[4-(3-hydroxy-propanoyl)-piperazin-1-yl]-phenyl}-amide;

or a pharmaceutically acceptable salt thereof 4-[4-({1-[6-Fluoro-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromen-2-yl]-methanoyl}-amino)-phenyl]-piperazine-1-carboxylic acid ethylamide;

6-Methoxy-8-(4-methyl-[1,4]diazepan-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (4-morpholin-4-yl-phenyl)-amide;

6-Ethoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (4-morpholin-4-yl-phenyl)-amide;

6-Ethoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid [4-(4-propionyl-piperazin-1-yl)-phenyl]-amide;

6-Methoxy-4-oxo-8-piperazin-1-yl-4H-chromene-2-carboxylic acid (4-morpholin-4-yl-phenyl)-amide;

6-Hydroxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (4-morpholin-4-yl-phenyl)-amide;

6-Methoxy-8-(4-methyl-[1,4]diazepan-1-yl)-4-oxo-1,4-dihydro-quinoline-2-carboxylic acid (4-morpholin-4-yl-phenyl)-amide;

540 - diazepan
541 - thiomorph

6-Fluoro-4-oxo-8-piperazin-1-yl-4*H*-chromene-2-carboxylic acid (4-morpholin-4-yl-phenyl)-
amide.

CLAIMSWe Claim:

1. A compound selected from: 8-(4-methyl-1-piperazinyl)-*N*-[4-(4-morpholinyl)phenyl]-4-oxo-4*H*-chromene-2-carboxamide;
2. {1-[4-(2-Methoxy-phenyl)-piperazin-1-yl]-methanoyl}-8-(4-methyl-piperazin-1-yl)-chromen-4-one;
- 2-{1-[4-(1-Acetyl-2,3-dihydro-1*H*-indol-6-yl)-piperazin-1-yl]-methanoyl}-8-(4-methyl-piperazin-1-yl)-chromen-4-one;
- 10 2-Chloro-5-(4-{1-[8-(4-methyl-piperazin-1-yl)-4-oxo-4*H*-chromen-2-yl]-methanoyl}-piperazin-1-yl)-benzonitrile;
- 2-{1-[4-(4-Methoxy-phenyl)-piperazin-1-yl]-methanoyl}-8-(4-methyl-piperazin-1-yl)-chromen-4-one;
- 8-(4-Methyl-piperazin-1-yl)-4-oxo-4*H*-chromene-2-carboxylic acid (5-furan-2-yl-1*H*-pyrazol-15 3-yl)-amide;
- 8-(4-Methyl-piperazin-1-yl)-4-oxo-4*H*-chromene-2-carboxylic acid (4-imidazol-1-yl-phenyl)-amide;
- 8-(4-Methyl-piperazin-1-yl)-4-oxo-4*H*-chromene-2-carboxylic acid (4-[1,2,3]thiadiazol-5-yl-phenyl)-amide;
- 20 8-(4-Methyl-piperazin-1-yl)-4-oxo-4*H*-chromene-2-carboxylic acid 4-[1,2,3]thiadiazol-5-yl-benzylamide;
- 8-(4-Methyl-piperazin-1-yl)-4-oxo-4*H*-chromene-2-carboxylic acid [4-(4-acetyl-piperazin-1-yl)-phenyl]-amide;
- 8-(4-Methyl-piperazin-1-yl)-4-oxo-4*H*-chromene-2-carboxylic acid [4-(4-methanesulfonyl-piperazin-1-yl)-phenyl]-amide;
- 25 8-(4-Methyl-piperazin-1-yl)-4-oxo-4*H*-chromene-2-carboxylic acid (2-methoxy-4-morpholin-4-yl-phenyl)-amide;
- 8-(4-Methyl-piperazin-1-yl)-4-oxo-4*H*-chromene-2-carboxylic acid (3-chloro-4-morpholin-4-yl-phenyl)-amide;
- 30 8-(4-Methyl-piperazin-1-yl)-4-oxo-4*H*-chromene-2-carboxylic acid (4-thiomorpholin-4-yl-phenyl)-amide;

8-(4-Methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (2,5-diethoxy-4-morpholin-4-yl-phenyl)-amide;

8-(4-Methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (4-cyanomethyl-phenyl)-amide;

5 8-(4-Methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (1H-indol-5-yl)-amide;

8-(4-Methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid [4-(1-morpholin-4-yl-methanoyl)-phenyl]-amide;

8-(4-Methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid [4-(2,6-dimethyl-morpholin-4-yl)-phenyl]-amide;

10 8-(4-Methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid [4-(4-fluoro-phenoxy)-phenyl]-amide;

8-(4-Methyl-piperazin-1-yl)-2-(6-morpholin-4-yl-benzooxazol-2-yl)-chromen-4-one;

8-(4-Methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (2-hydroxy-4-morpholin-4-yl-phenyl)-amide;

15 8-(4-Methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (5-ethoxy-benzothiazol-2-yl)-amide;

8-(4-Methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (4-bromo-phenyl)-amide;

8-(4-Methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid methyl-(4-morpholin-4-yl-phenyl)amide;

20 8-(4-Methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (3-morpholin-4-yl-phenyl)-amide;

8-(4-Methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (3-cyano-4-morpholin-4-yl-phenyl)-amide;

8-(4-Methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-amide;

25 4-[4-({1-[8-(4-Methyl-piperazin-1-yl)-4-oxo-4H-chromen-2-yl]-methanoyl}-amino)-phenyl]-piperazine-1-carboxylic acid *tert*-butyl ester;

8-(4-Methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (4-piperazin-1-yl-phenyl)-amide;

30 6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (4-morpholin-4-yl-phenyl)-amide;

- 6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid [4-(4-methanesulfonyl-piperazin-1-yl)-phenyl]-amide;
- 6-Methoxy-8-(4-Methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (3-chloro-4-morpholin-4-yl-phenyl)-amide;
- 5 6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-amide;
- 6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (2-methoxy-4-morpholin-4-yl-phenyl)-amide;
- 6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (4-thiomorpholin-4-yl-phenyl)-amide;
- 10 6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid [4-(2,6-dimethyl-morpholin-4-yl)-phenyl]-amide;
- 6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (3-morpholin-4-yl-phenyl)-amide;
- 15 6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid {4-[4-(2-hydroxy-ethyl)-piperazin-1-yl]-phenyl}-amide;
- 6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid [4-(1-morpholin-4-yl-methanoyl)-phenyl]-amide;
- 6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (3-cyano-4-morpholin-4-yl-phenyl)-amide;
- 20 4-[4-({1-[6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromen-2-yl]-methanoyl}-amino)-phenyl]-piperazine-1-carboxylic acid *tert*-butyl ester
- 6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (4-piperazin-1-yl-phenyl)-amide;
- 25 6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid [4-(4-propionyl-piperazin-1-yl)-phenyl]-amide;
- 6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid [4-(4-ethane sulfonyl-piperazin-1-yl)-phenyl]-amide;
- 6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid [4-(4-dimethyl sulfamoyl-piperazin-1-yl)-phenyl]-amide;
- 30 4-[4-({1-[6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromen-2-yl]-methanoyl}-amino)-phenyl]-piperazine-1-carboxylic acid dimethylamide;

- Q1 cont*
- 4-[4-({1-[6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromen-2-yl]-methanoyl}-amino)-phenyl]-piperazine-1-carboxylic acid ethylamide;
- 4-[4-({1-[6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromen-2-yl]-methanoyl}-amino)-phenyl]-piperazine-1-carboxylic acid cyclohexylamide;
- 5 4-[4-({1-[6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromen-2-yl]-methanoyl}-amino)-phenyl]-piperazine-1-carboxylic acid cyclopentylamide;
- 6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid {4-[4-(1-pyrrolidin-1-yl-methanoyl)-piperazin-1-yl]-phenyl}-amide;
- 6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid {4-[4-(propane-2-sulfonyl)-piperazin-1-yl]-phenyl}-amide;
- 10 6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid {4-[4-(2-methyl-propanoyl)-piperazin-1-yl]-phenyl}-amide;
- 6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid {4-[4-(1-morpholin-4-yl-methanoyl)-piperazin-1-yl]-phenyl}-amide;
- 15 6-Fluoro-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (4-morpholin-4-yl-phenyl)-amide;
- 6-Fluoro-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid [4-(4-methanesulfonyl-piperazin-1-yl)-phenyl]-amide;
- 6-Fluoro-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid [4-(4-acetyl-piperazin-1-yl)-phenyl]-amide;
- 20 6-Fluoro-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (3-chloro-4-morpholin-4-yl-phenyl)-amide;
- 6-Fluoro-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-amide;
- 25 6-Fluoro-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (3-cyano-4-morpholin-4-yl-phenyl)-amide;
- 6-Fluoro-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid [4-(1-morpholin-4-yl-methanoyl)-phenyl]-amide;
- 6-Methyl-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (4-morpholin-4-yl-phenyl)-amide;
- 30 6-Methyl-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid [4-(1-morpholin-4-yl-methanoyl)-phenyl]-amide;

~~6-Methyl-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-amide;~~

~~6-Chloro-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (4-morpholin-4-yl-phenyl)-amide;~~

5 5-Methyl-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (4-morpholin-4-yl-phenyl)-amide;

5-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (4-morpholin-4-yl-phenyl)-amide;

6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid {4-[4-(3-hydroxy-propanoyl)-piperazin-1-yl]-phenyl}-amide;

10 4-[4-({1-[6-Fluoro-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromen-2-yl]-methanoyl}-amino)-phenyl]-piperazine-1-carboxylic acid *tert*-butyl ester;

4-[4-({1-[6-Fluoro-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (4-piperazin-1-yl-phenyl)-amide;

15 6-Fluoro-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid [4-(4-ethane sulfonyl-piperazin-1-yl)-phenyl]-amide;

6-Fluoro-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid [4-(4-propionyl-piperazin-1-yl)-phenyl]-amide; and

6-Fluoro-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid {4-[4-(3-hydroxy-propanoyl)-piperazin-1-yl]-phenyl}-amide;

20 or a pharmaceutically acceptable salt thereof.

2. A compound selected from: 8-(4-methyl-1-piperazinyl)-*N*-[4-(4-morpholinyl)phenyl]-4-oxo-4*H*-chromene-2-carboxamide;

25 6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (4-morpholin-4-yl-phenyl)-amide;

6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid [4-(4-propionyl-piperazin-1-yl)-phenyl]-amide;

6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid [4-(4-ethane sulfonyl-piperazin-1-yl)-phenyl]-amide;

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6-Fluoro-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid [4-(4-acetyl-piperazin-1-yl)-phenyl]-amide;

6-Fluoro-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid [4-(4-ethanesulfonyl-piperazin-1-yl)-phenyl]-amide; and

6-Fluoro-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid [4-(4-propionyl-piperazin-1-yl)-phenyl]-amide;

5 or a pharmaceutically acceptable salt thereof.

3. 8-(4-methyl-1-piperazinyl)-*N*-[4-(4-morpholinyl)phenyl]-4-oxo-4H-chromene-2-carboxamide; or a pharmaceutically acceptable salt thereof.

10 4. 6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid (4-morpholin-4-yl-phenyl)-amide; or a pharmaceutically acceptable salt thereof.

5. 6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid [4-(4-propionyl-piperazin-1-yl)-phenyl]-amide; or a pharmaceutically acceptable salt thereof.

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6. 6-Methoxy-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid [4-(4-ethane sulfonyl-piperazin-1-yl)-phenyl]-amide; or a pharmaceutically acceptable salt thereof.

7. 6-Fluoro-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid [4-(4-acetyl-piperazin-1-yl)-phenyl]-amide; or a pharmaceutically acceptable salt thereof.

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8. 6-Fluoro-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid [4-(4-ethanesulfonyl-piperazin-1-yl)-phenyl]-amide; or a pharmaceutically acceptable salt thereof.

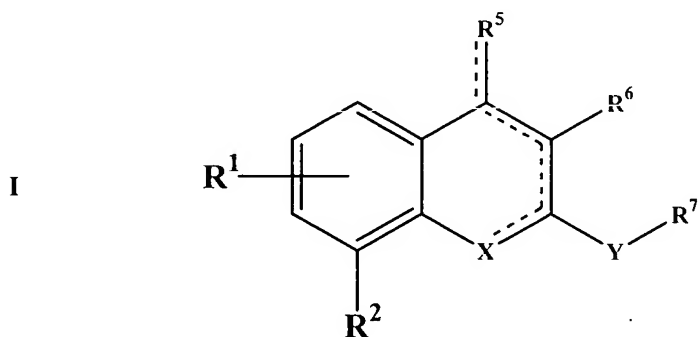
25 9. 6-Fluoro-8-(4-methyl-piperazin-1-yl)-4-oxo-4H-chromene-2-carboxylic acid [4-(4-propionyl-piperazin-1-yl)-phenyl]-amide; or a pharmaceutically acceptable salt thereof.

A B S T R A C T

TITLE: THERAPEUTIC HETEROCYCLIC COMPOUNDS

5

Provided herein is a compound having the formula (I):



Wherein said compounds are useful for the treatment of psychiatric disorders including but
10 not limited to depression, generalized anxiety, eating disorders, dementia, panic disorder, and
sleep disorders. The compounds may also be useful in the treatment of gastrointestinal
disorders, cardiovascular regulation, motor disorders, endocrine disorders, vasospasm and
sexual dysfunction. The compounds are 5HT_{1B} and 5HT_{1D} antagonists.

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